

# PATENT COOPERATION T RY

**PCT**

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 12 May 2000 (12.05.00)	
<b>International application No.</b> PCT/US99/17931	<b>Applicant's or agent's file reference</b> PCT 20276
<b>International filing date</b> (day/month/year) 10 August 1999 (10.08.99)	<b>Priority date</b> (day/month/year) 14 August 1998 (14.08.98)
<b>Applicant</b> LOWE, Robert, S. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
14 March 2000 (14.03.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland	<b>Authorized officer</b> Claudio Borton
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b> <b>A61K 39/12, 48/00, C07H 21/02, 21/04,</b> <b>C12N 5/10, 7/01, 7/04, 15/37, 15/86</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 00/09157</b> <b>(43) International Publication Date:</b> 24 February 2000 (24.02.00)
<b>(21) International Application Number:</b> PCT/US99/17931 <b>(22) International Filing Date:</b> 10 August 1999 (10.08.99) <b>(30) Priority Data:</b> 60/096,638 14 August 1998 (14.08.98) US <b>(71) Applicant (for all designated States except US):</b> MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> LOWE, Robert, S. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). JANSEN, Kathrin, U. [DE/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). JOYCE, Joseph, G. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). MCCLEMENTS, William, L. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). COOK, James, C., III [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). LING, Jessica, Ching-Yee [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). NEEPER, Michael, P. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).		<b>(74) Common Representative:</b> MERCK & CO., INC.; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). <b>(81) Designated States:</b> AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> PROTEIN DELIVERY SYSTEM USING HUMAN PAPILLOMAVIRUS VIRUS-LIKE PARTICLES <b>(57) Abstract</b> <p>Human Papillomavirus virus like particles (VLPs) have been constructed so that they contain a modified L2 protein. The L2 protein has been minimized and is fused to a second protein or peptide. The fused protein is incorporated into the VLP and the VLP can deliver the protein to a cell. The modified VLPs can be used to increase the breadth of immune response in vaccine preparations or to deliver other proteins of interest.</p>		

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Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 12 JUL 2000

PCT

Applicant's or agent's file reference 20276PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/17931	International filing date (day/month/year) 10 AUGUST 1999	Priority date (day/month/year) 14 AUGUST 1998
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant MERCK & CO., INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 14 MARCH 2000	Date of completion of this report 19 MAY 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer <i>David Guzo</i> DAVID GUZO
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/17931

**I. Basis of the report****1. With regard to the elements of the international application:\***

- ☒ the international application as originally filed
- ☒ the description:  
pages 1-14 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_
- ☒ the claims:  
pages 15-16 , as originally filed  
pages NONE , as amended (together with any statement) under Article 19  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_
- ☒ the drawings:  
pages 1-4 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_
- ☒ the sequence listing part of the description:  
pages 1-2 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:**

- ☒ contained in the international application in printed form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

**4. ☒ The amendments have resulted in the cancellation of:**

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig NONE

**5. ☒ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\***

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/17931

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. statement**

Novelty (N)	Claims <u>1-12</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>1-12</u>	YES
	Claims <u>NONE</u>	NO
Industrial Applicability (IA)	Claims <u>1-12</u>	YES
	Claims <u>NONE</u>	NO

**2. citations and explanations (Rule 70.7)**

Claims 1-12 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the claimed nucleic acids encoding fusion peptides between a less than full length HPV L2 protein and a second peptide, HPV virus like particles containing said fusion peptides, host cells containing said HPV virus-like particles, vaccines containing said particles and a method of delivering said fusion peptides to target cells.

It is noted that the Lowy et al. U.S. Patent 5,855,891 was previously indicated by the examiner to be an anticipatory reference (X reference on the Search Report). This was in error because the issue date of the Lowy et al. patent was after the priority date granted in the instant application. Also, Lowy et al. does not teach using a less than full length HPV L2 protein in the fusion constructs.

----- NEW CITATIONS -----  
NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/17931

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): A61K 39/12, 48/00; C07H 21/02, 21/04; C12N 5/10, 7/01, 7/04, 15/37, 15/86 and US Cl.: 424/204.1, 93.2, 93.6; 514/2, 44; 435/455, 456, 320.1, 325, 366

**I. BASIS OF REPORT:**

5. (Some) amendments are considered to go beyond the disclosure as filed:

NONE

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/17931**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : Please See Extra Sheet.

US CL : 424/204.1, 93.2, 93.6; 514/2, 44; 435/455, 456, 320.1, 325, 366

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/204.1, 93.2, 93.6; 514/2, 44; 435/455, 456, 320.1, 325, 366

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WEST, Dialog, Medline, Biosis, Biotech

Search terms: papillomavirus, L2, fusion, vaccine, L1, virus-like particle

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,618,536 A (LOWY et al.) 08 April 1997, columns 7-8 and claims 1-10.	5-7
A	US 5,437,951 A (LOWY et al.) 01 August 1995, columns 3-4.	1-12
A,P	US 5,855,891 A (LOWY et al.) 05 January 1999, columns 5-6.	1-12

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*E* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Z* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

20 DECEMBER 1999

Date of mailing of the international search report

03 FEB 2000

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

DAVID GUZO

Telephone No. (703) 308-0196



# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/17931

## A. CLASSIFICATION OF SUBJECT MATTER: IPC (6):

A61K 39/12, 48/00; C07H 21/02, 21/04; C12N 5/10, 7/01, 7/04, 15/37, 15/86